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## Effect of Acute Posttransplant Renal Failure on the Survival of Perfused Cadaver Kidneys\*

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*Between 1973 and 1977 we encountered 22 cases of acute renal failure after transplantation in 70 patients who received perfused cadaver kidneys. Nearly two-thirds of 16 nonfunctioning grafts were lost due to subsequent superimposed rejection, often undetected and, hence, untreated. Thirty-one percent of the 16 recovered function. The recovery rate, we believe, can be improved by earlier diagnosis and treatment of rejection and by avoiding invasive diagnostic procedures in the early postoperative period. If the oliguric period extends beyond two weeks, a closed percutaneous renal biopsy is justified. The diagnosis of rejection and/or other abnormality as well as subsequent treatment are very important in these patients.*

ACUTE tubular necrosis occurs frequently after transplantation of cadaver kidneys undergoing ischemia or prolonged preservation.<sup>1</sup> Toledo-Pereyra et al<sup>2,3</sup> found no difference in the functional survival rate between perfused grafts with acute tubular necrosis and those that functioned immediately after transplantation. Similar findings were reported in a separate study from the University of Minnesota by Kjellstrand and associates<sup>4</sup> with perfused or fresh cadaver grafts. However, others such as Baxby<sup>5</sup> and Whittaker<sup>6</sup> have reported a high failure rate with grafts that showed acute tubular necrosis immediately after transplantation. This paper analyzes our experience with acute posttransplant renal failure in perfused cadaver kidney transplants.

### Patients

All patients who received transplants of perfused cadaver kidneys at Henry Ford Hospital between July 1, 1973 and June 30, 1977 were reviewed on January 1, 1978. The follow-up period after transplantation was a minimum of six months, the average time being 24 months. Of 70 patients, 48 had immediate renal function. Twenty-two recipients (31%) showed no immediate function, and continued dialysis was necessary because of increasing uremia after transplantation. Six of the 22 patients had technical complications and were not included in the final comparison. The remaining 16 patients with acute posttransplant renal failure were compared with those whose kidneys functioned immediately after transplantation.

### Methods

Standard methods of harvesting were employed in all cadaver kidneys, which were preserved by hypothermic pulsatile perfusion with cryoprecipitated plasma for variable periods of time. The surgical transplant technique, immunosuppression, and postoperative treatment remained constant throughout the study. Recipient immunosuppressive dosages consisted of azathioprine 5.0 mg/kg/day for one day, then 2.0 mg/kg/day for 14 days,

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then 1.0-2.0 mg/kg/day, adjusted according to the white blood count. Prednisolone was given in a dose of 1.2 mg/kg/day on the day of surgery, with the total dose then reduced by 2.0 mg each day to a maintenance dose of 10 to 30 mg daily. There was no difference in medication between the patients with acute graft failure and those with immediately functioning grafts. For rejection episodes, patients were treated with one gram of intravenously administered methylprednisolone for each of three days.

When dialysis was necessary, it was performed daily or every other day after transplantation for four hours. Regional heparinization was used in all instances.

### Diagnostic procedures in posttransplant oliguria

If there was no diuresis in the adequately hydrated transplant patient, a renogram was performed. Five millicuries of Tc99m sulfur colloid were given intravenously; 20 to 30 minutes later an anterior image was taken over the area of the transplanted kidney in order to discover accumulation of activity in the transplant. Three hundred thousand counts were accumulated. Next, ten millicuries of Tc99m-Sn-DTPA were injected intravenously in an antecubital vein. Flow images were generated every two seconds by a computer for two minutes; a static image was taken during the flow study and also one hour after the injection. A time/activity curve was generated for the flow through the kidney. In some cases aortorenal transit time was calculated. This step was then followed by a  $^{131}\text{I}$  Hippuran renogram, during which four hundred microcuries of  $^{131}\text{I}$  Hippuran were injected intravenously (bolus technique). Computer images were taken every minute for twenty minutes from a region of interest placed over the transplant, and another probe was placed

over the bladder. Time/activity graphs were generated showing the flow change in the kidney and the bladder.

If the renogram showed poor uptake, a renal arteriogram was performed to rule out vascular occlusion or intrarenal thrombosis. If the renal arteriogram showed evidence of occluding thrombosis, surgical exploration was performed. A normal renogram was not usually followed by further invasive diagnostic studies except for follow-up serial renograms, which were obtained approximately every four to seven days in these patients. If progressive return of renal function was not apparent, renal biopsies were performed in a selected group of patients. The diagnosis of rejection was made mainly on clinical grounds, i.e., graft swelling, tenderness, fever, and, in the case of functioning grafts, a rise in the serum creatinine and diminished urine output.

The actuarial survival of all kidneys was calculated by the method of Merrell and Shulman.<sup>7</sup> Fisher's exact probability test was also used for statistical analysis.

### Results

Of the 16 grafts that did not function immediately after transplantation, five (31%) recovered function. Three of these are still functioning over three years since transplantation, and two are surviving after a six-month follow-up period. Average time for recovery was 18 days (varying from 13 to 24 days) with an average of four dialysis treatments (ranging from 1 to 6). Nine of the remaining eleven grafts underwent nephrectomy at a mean of 25 days after transplantation (range: 4-48 days). Nephrectomy was indicated if a biopsy revealed renal destruction, due probably to rejection episodes<sup>5</sup> and severe infection originating from the

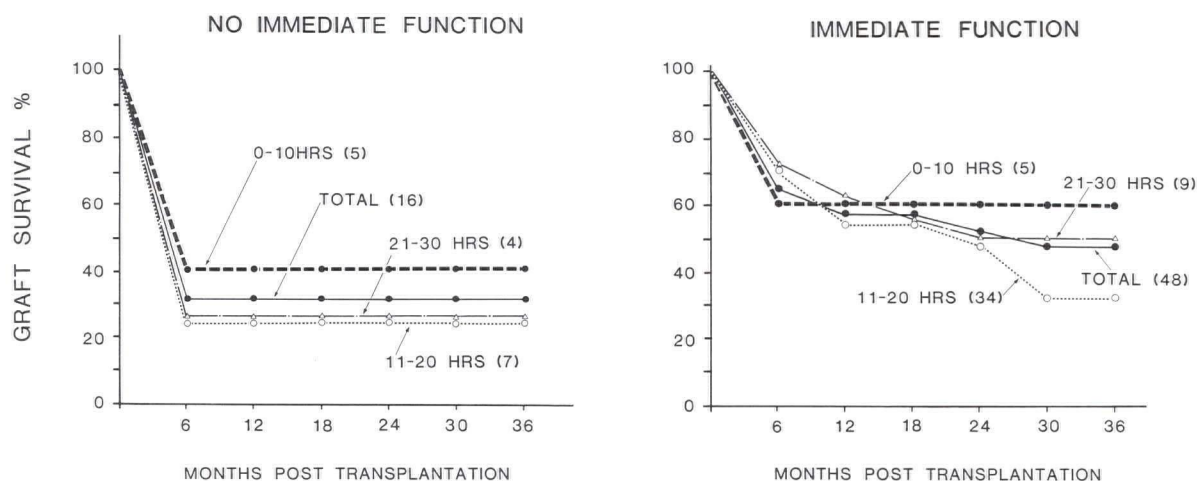


Fig. 1

Actuarial functional survival rate in patients whose grafts functioned immediately and those that did not, divided according to the length of perfusion. Grafts that function immediately have a better survival rate.



## Posttransplant Renal Failure in Perfused Cadaver Kidneys

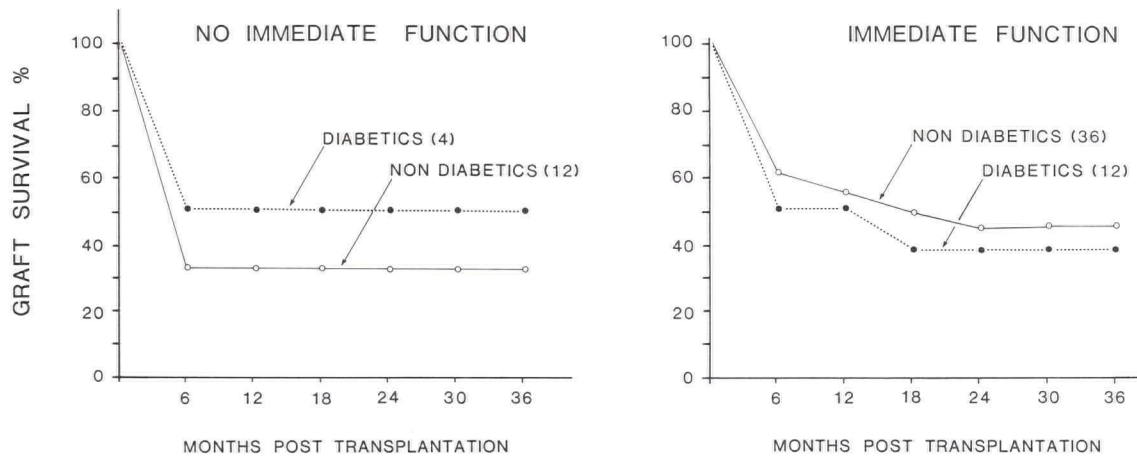


Fig. 2

Actuarial functional survival rate in diabetic and nondiabetic patients. Diabetes does not seem to affect either immediately functioning or nonfunctioning grafts.

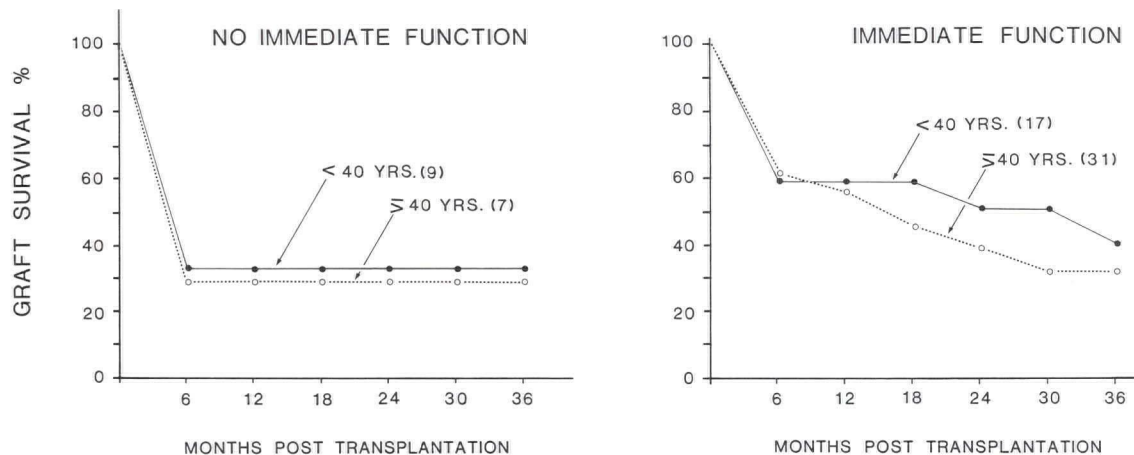


Fig. 3

Effect of age on the actuarial functional survival rate of immediately functioning and nonfunctioning kidneys is minimal.

graft.<sup>4</sup> In the two remaining cases, one patient died of sepsis on the 15th postoperative day without recovering kidney function, while the other patient still has his nonfunctional graft.

Figure 1 represents the actuarial functional survival rate of the grafts with or without immediate function, divided according to the length of perfusion. Presently 31% of the group with acute posttransplant renal failure are functioning versus 47% of those grafts that functioned immediately. It is apparent from our study that perfused cadaver kidneys with immediate function had a better chance of survival than those which did not. The length of perfusion did not seem to have any effect on survival.<sup>8</sup>

Other factors that might affect graft survival are indicated in Figures 2-5. These include diabetes (Figure 2), age (Figure 3),

number of transplants (Figure 4), and sex (Figure 5). Figure 6 shows that good HLA antigen matching markedly improved the survival rate in both immediately functioning and nonfunctioning grafts, although these findings were not statistically significant ( $p > 0.1$ ).

Of the 16 kidneys which did not function immediately, ten suffered clinically detectable rejection within the first month after transplantation. The average number of rejections per patient was 0.875. All five grafts which recovered function had been treated for one to three rejection episodes, and the overall survival rate of those which suffered rejections was 50%. Of the 48 immediately functioning grafts, 35 (73%) suffered rejection episodes. The average number of rejections per patient was 2.0.

Figures 7 and 8 illustrate a typical case of acute post-

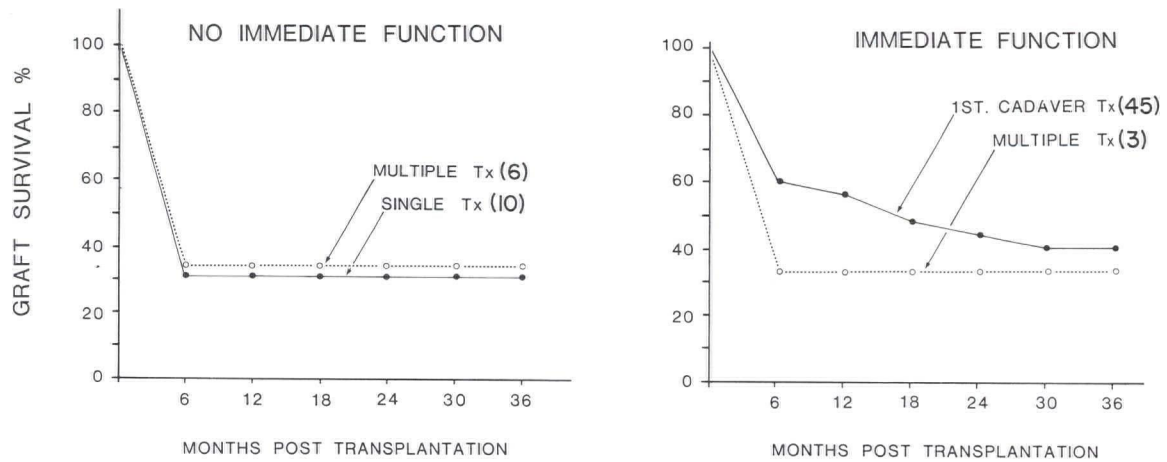


Fig. 4

Actuarial functional survival rates in patients with first cadaver transplants. The number of transplants did not influence the proportion of grafts lost in both groups.

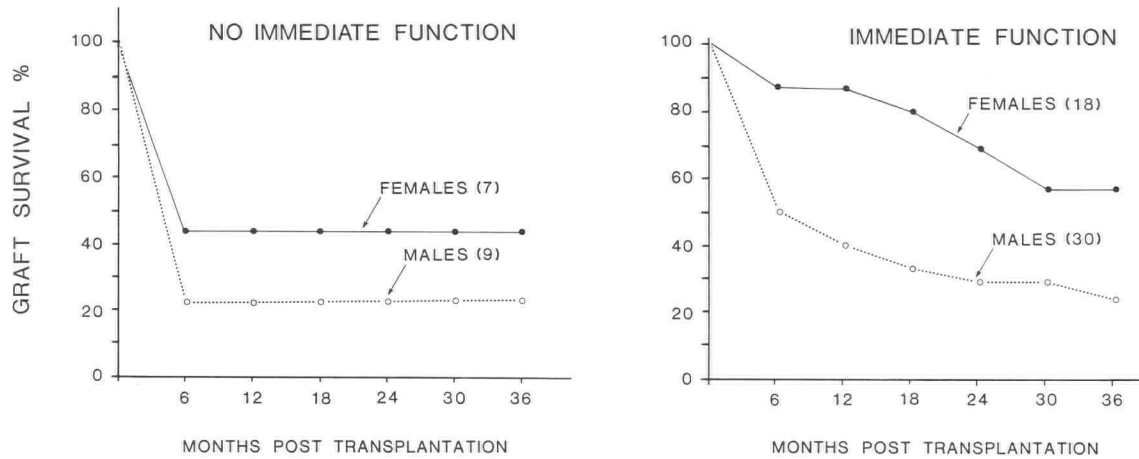


Fig. 5

Effect of sex on the actuarial functional survival rate. Female recipients had better survival rates than males.

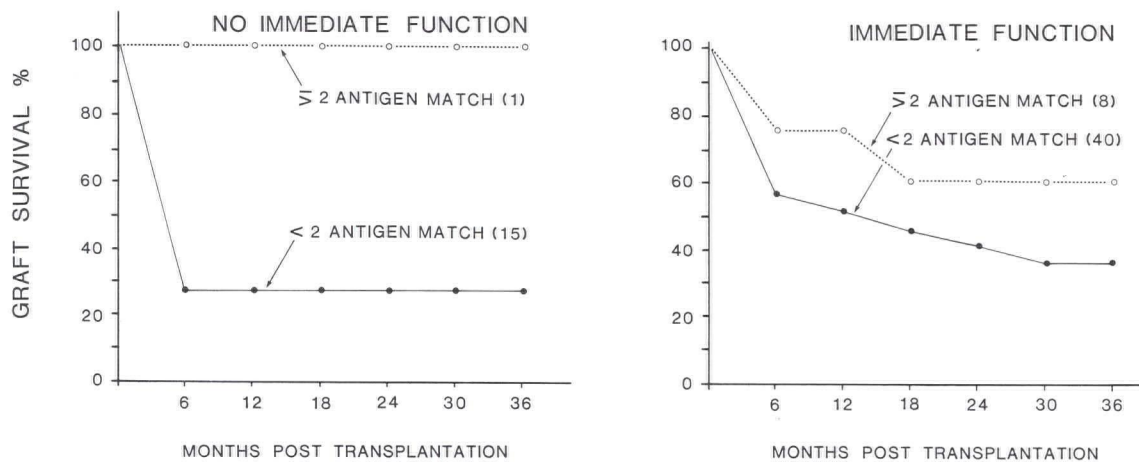


Fig. 6

Actuarial functional survival rate of antigen matching for immediately functioning and nonfunctioning grafts. Closer antigen matching markedly improves the survival rate.

## Posttransplant Renal Failure in Perfused Cadaver Kidneys

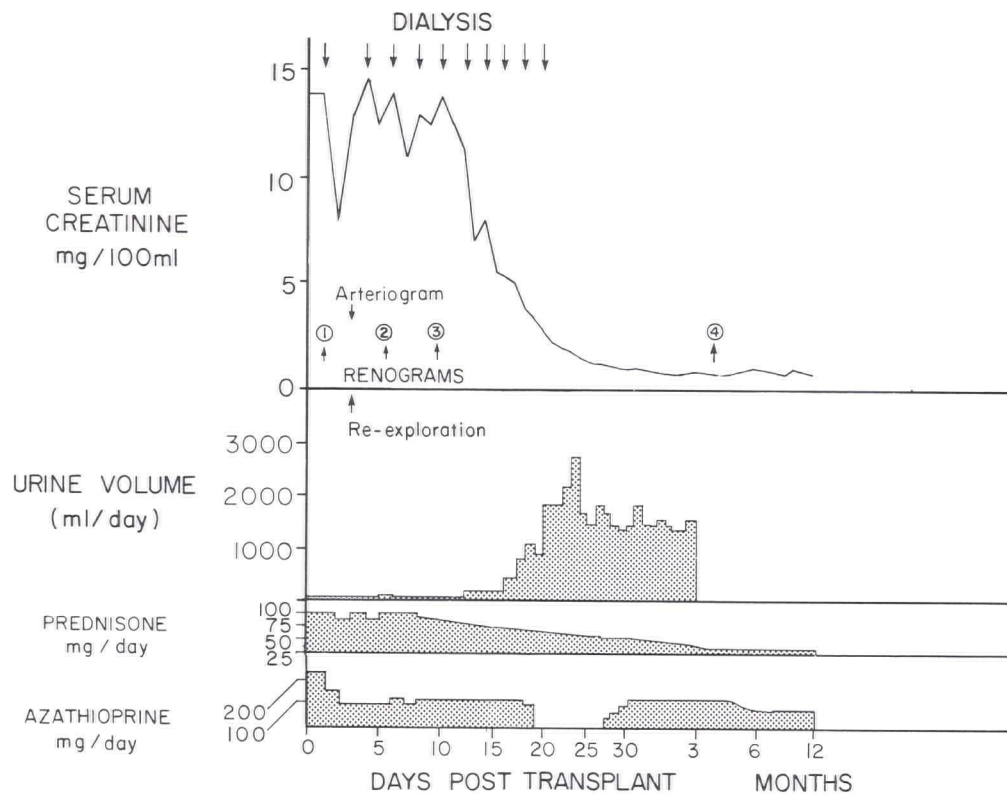


Fig. 7

Acute posttransplant renal failure in a patient who received a perfused cadaver kidney. Frequent dialysis under regional heparinization was used. Urine output gradually increased with a corresponding decline in serum creatinine toward normal after three weeks.

transplant renal failure. Four renograms were taken. Those obtained on days 2 and 6 show a well perfused transplanted kidney with good uptake of Tc99m sulfur colloid and evidence of intrarenal obstruction by a marked retention of Hippuran; these findings are consistent with acute tubular necrosis. The renogram on the 11th postoperative day showed similar findings, although there was significantly increased colloid accumulation in the transplant. One month after transplantation the renogram was normal, showing good perfusion and excretion of the radionuclide. An arteriogram (Figure 9) taken on the third postoperative day demonstrated a normal vascular pattern except for kinking of the renal artery, which was surgically corrected on the same day.

There were three deaths in the group without immediate function. Two patients died of sepsis, one died on the 15th postoperative day, and the other died 20 days after nephrectomy had been performed on the 15th posttransplant day for persistent acute tubular necrosis with superimposed rejection. The last patient, who had had a transplant nephrectomy on the 4th postoperative day, died 45 days after transplantation of massive gastrointestinal bleeding.

## Discussion

Our study indicates that acute posttransplant renal failure in perfused cadaver kidneys had some detrimental effect on long-term graft function. In an attempt to explain this, several possibilities may be considered. First, we included all nonfunctioning kidneys under the category of acute posttransplant renal failure. In these patients rejection can very easily be masked by acute renal failure and, hence, go untreated. For instance, all five grafts which recovered function had been treated for one or more episodes of suspected rejection. In addition, six of the grafts that were nephrectomized showed, by histology, evidence of rejection superimposed on acute tubular necrosis. Second, our patients in general did not receive a third drug therapy associated with azathioprine and prednisone. Toledo-Perceyra<sup>2,3</sup> and Kjellstrand<sup>4</sup> reported that one reason for their good results in grafts with acute tubular necrosis was the routine use of high doses of antilymphoblast globulin in the initial posttransplant period, which offers some protection against rejection. Third, the complications which arise from multiple diagnostic procedures performed in nonfunctioning kidneys may contribute to the poor survival rate in this



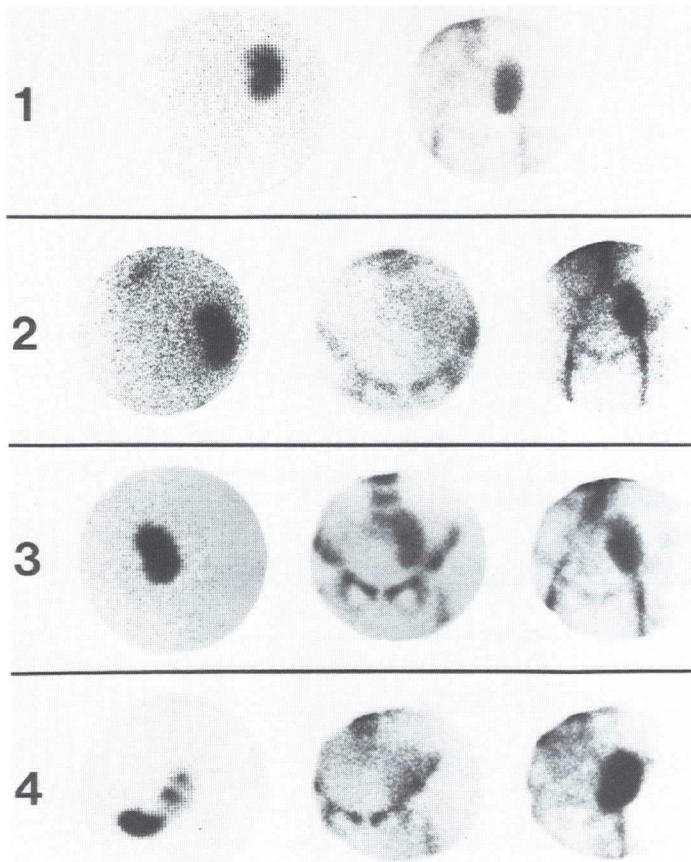


Fig. 8

Renograms of case illustrated in Figure 7. The numbers refer to the corresponding number on the graph in Figure 7. There was immediate good uptake on the renogram on all examinations.

group of patients.<sup>4,6</sup> This, however, was not a factor in our series. The incidence of acute posttransplant renal failure at our institution is comparable to that reported by many others.<sup>1,2,4,9,10</sup>

We believe that, if posttransplant oliguria occurs, a renogram should be performed within a few hours after surgery. If this shows good perfusion of the graft, no further invasive diagnostic procedures should be carried out at this early stage. If poor uptake is evident, a renal arteriogram should be performed to rule out vascular occlusion or evidence of intrarenal thrombosis secondary to hyperacute or accelerated rejection. If the arteriogram shows a relatively normal arterial tree, no further invasive diagnostic studies should be performed. However, if there is evidence of arterial thrombosis or hyperacute rejection, surgical exploration and possibly nephrectomy are indicated.

Other invasive diagnostic tools, such as "second-look" operations, routine renal arteriograms, and retrograde pyelography, should be used very cautiously. We believe these procedures are dangerous for the immunosuppressed patient who requires dialysis. If, however, oliguria persists beyond two weeks, a closed percutaneous renal biopsy is justified to decide whether to continue the present treatment, to treat for rejection, or to perform a nephrectomy.

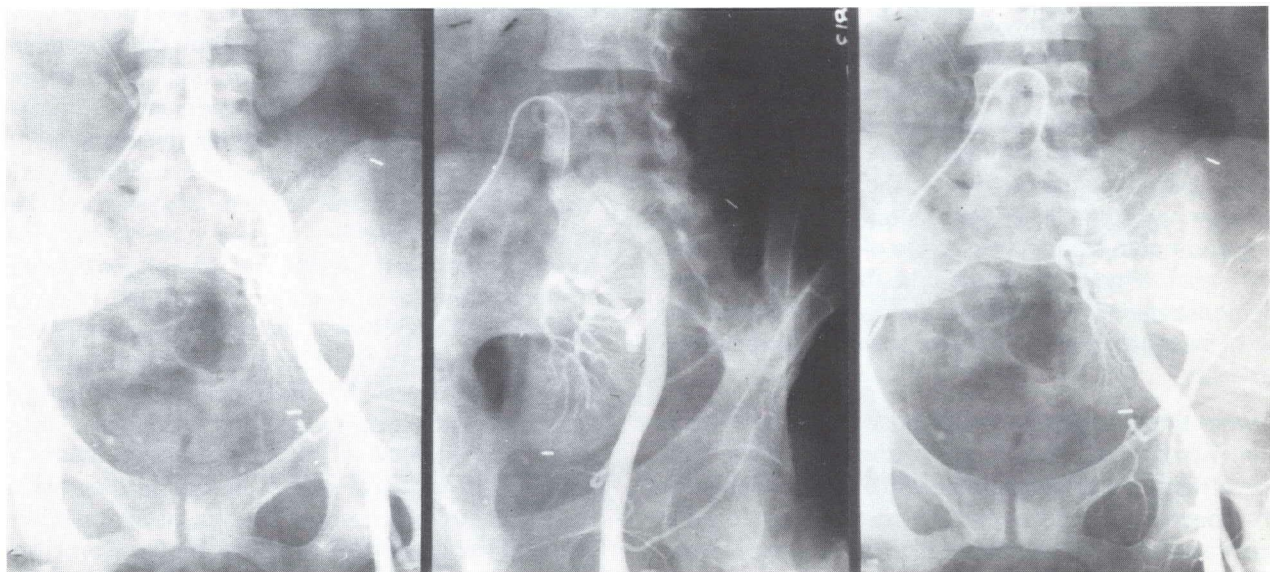


Fig. 9

Arteriogram of the patient in Figure 7 shows normal perfusion except for kinking of the renal artery, which was surgically corrected.



### Acknowledgments

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